

REMARKS/ARGUMENTS

Claims 40-48, 112-119, 121, 123 and 124 are pending in the application. Claims 40-48, 112-119, 121, 123 and 124 are objected to and rejected. Applicants submit a Supplemental Information Disclosure Statement herewith, including the requisite fee, in view of issues raised by the Examiner during the prosecution of this case.

Applicants thank Examiner Qian and Examiner Falk for their time and consideration during the telephonic interview with Applicants' representative, Melissa Sistrunk, on July 16, 2003 regarding outstanding matters set forth in the Office Action. Specifically discussed issues during the interview are addressed herein.

Issues Regarding Claim Objections

Claims 40-48, 112-119, 121, 123 and 124 are objected to in the present application. The Examiner objects to the currently pending claims as containing non-elected subject matter. The Examiner alleges that the claims, currently encompassing SEQ ID NO:70, are objectionable in that SEQ ID NO:58 was elected for examination in previous correspondence. The Examiner furthermore states that the claims should be amended such that they are directed to elected inventions only. Applicants respectfully disagree with this objection.

Based on the telephonic interview of July 16, 2003, it is Applicants' understanding from the Examiners that an objection to a non-elected invention in the context of this case is not proper in view of the inclusion of SEQ ID NO:70 within SEQ ID NO:58. Applicants further note that the respective element "...comprises at least about 80% identity to SEQ ID NO:70" is described in the specification (paragraph beginning on page 33, line 15), and the nature of the sequence was well known at the time of filing (Jarman et al., 1993, already of record). Utilizing this particular *atonal*-associated sequence for generating hair cells in an animal is well enabled by the specification, particularly since SEQ ID NO:70 merely is a portion included in the larger sequence of SEQ ID NO:58 to which the Examples are analogously related. Therefore, the claims including this particular element are both well described at the time of filing and clearly enabled.

Applicants respectfully request removal of the objection.

Issues Regarding 35 U.S.C. §112, paragraph 1

The Examiner continues to reject claims 40-48, 112-119, 121, 123 and 124 for allegedly not being enabled. Applicants respectfully disagree, however, and have amended claims 45 and 124 and cancelled claims 47, 115, and 116 to further the prosecution of the instant application. Thus, the amendments are submitted without prejudice and without acquiescence, and Applicants reserve the right to pursue these elements in future prosecution.

The Examiner contends (such as in the Office Action beginning on page 4) that there is no nexus between hearing restoration and hair cell generation. However, the pending claims are directed to a method of generating hair cells, a composition, and a nucleic acid sequence. MPEP § 2164 states “the invention that one skilled in the art must be enabled to make and use is that defined by the claim(s) of the particular application (emphasis added).” The presently pending claims do not require restoration of hearing, but recite a method to generate hair cells, a composition comprising an *atonal*-associated nucleic acid in combination with a delivery vehicle, and a nucleic acid sequence encoding a fusion protein comprising an *atonal*-associated amino acid sequence or fragment thereof and a desired amino acid sequence. Therefore, the continued rejection of the claims under the standard of restoration of hearing and balance is unmerited and improper.

The specification teaches the generation of hair cells by administering an *atonal*-associated nucleic acid sequence to the ear at, for example, page 8, lines 8-15. In this regard, Applicants note that actual reduction to practice prior to filing is not required to prove enablement. *In re Gould v. Quigg*, 822 F.2d 1074, 1078, 3 USPQ 2d 1302, 1304 (Fed. Cir. 1987). Furthermore, it is well-settled case law that a specification need not contain an example if the invention is otherwise disclosed in such a manner that one skilled in the art will be able to practice it without an undue amount of experimentation. *In re Borkowski*, 422 F.2d 904, 908, 164 USPQ 642, 645 (CCPA 1970). No undue experimentation is required to make and use the invention as claimed, given that others generated hair cells using *Math1*, an *atonal*-associated nucleic acid sequence, soon after Applicants’ filing date. Furthermore, pursuant to the teachings of Applicants’ specification, others in the art generated hair cells following delivery of *atonal*-associated sequences into the inner ear of mammals (Kawamoto et al., 2003; Shou et al., 2003; both submitted herewith).

Upon and near the time of filing, those of skill in the art were aware that expression of *atonal* resulted in hair cell generation and/or auditory organs. For example, Applicants state in the specification on Page 91, lines 2-5:

Math1 expression in flies, like *ato*, produced ectopic chordotonal organs (Fig. 8G), although with less efficiency. Overexpression of the *AS-C* genes does not, however, result in ectopic chordotonal organs (Jarman et al., 1993). *Math1* thus has a similar functional specificity to *ato*.

Furthermore, Zheng and Gao (2000; already of record) illustrated that *Math1* was sufficient for the production of hair cells in the ear. Therefore, given that hair cells/hearing organs have been generated with this invention and by others after the filing of the instant application, Applicants state that it would not be unpredictable nor elicit undue experimentation to practice the claimed invention. For these reasons alone, the rejection under Section 112, first paragraph, should be withdrawn.

Moreover, to address the comments set forth in the Office Action, the link between hair cells and hearing is well-known in the art, as demonstrated in the standard text excerpt from Anatomy & Physiology, 4th ed. (submitted in the Supplemental IDS herewith): “The stimulation, or “trigger” responsible for hearing and balance involves activation of specialized mechanoreceptors called *hair cells*.” Furthermore, the link between hair cell generation and restoration of function has been established in avian models wherein hair cells naturally regenerate following trauma. For example, Dooling *et al.*, *PNAS USA*, 94, 14206-14210 (1997), submitted herewith, reports that auditory perception in budgerigars was impaired upon chemical-induced damage of hair cells. Restoration of hearing coincided with hair cell regeneration. Likewise, Carey *et al.*, *J. Neurophysiol.*, 76, 3301-3312 (1996), submitted herewith, reports that hair cell regeneration contributed to the recovery of vestibuloocular reflex (VOR) in Leghorn chicks. Thus, it has been demonstrated that hair cell regeneration in the ear restores hearing and vestibular function (*e.g.*, balance) *in vivo*.

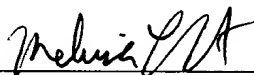
In light of the references available prior to the filing of the instant application, the nexus between hearing restoration and balance and hair cell generation has been established. As such, restoration of function using the inventive method is not unpredictable, particularly as others in the art have identified an analogous connection between hair cell generation and hearing restoration.

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding objection and rejection of the claims and to pass this application to issue.

Applicant believes no fee is due with this response other than the fee required for the Supplemental Information Disclosure Statement filed herewith. However, if another fee is due, please charge our Deposit Account No. 06-2375, under Order No. HO-P01899US2 from which the undersigned is authorized to draw.

Dated: July 29, 2003

Respectfully submitted,

By  _____

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